

10/795,795

STN Seq Search

XX 3-10 76 Seq Ids 6+12

EFD: July 23, 2001 (23.7.2001)

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

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* The CA roles and document type information have been removed from *
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* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
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Structure search iteration limits have been increased. See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
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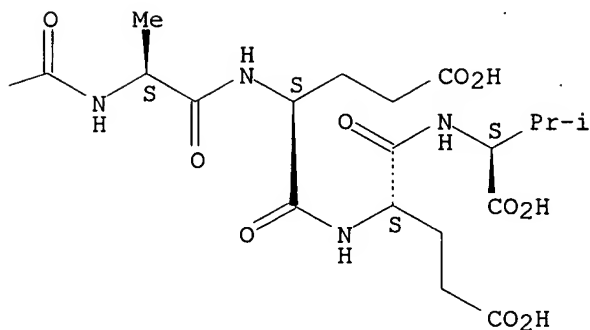
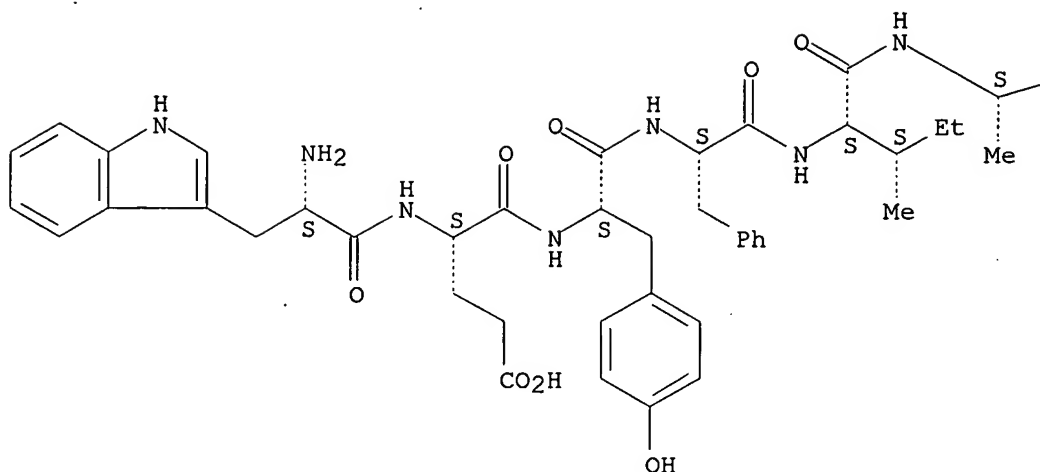
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      583950 3-10/SQL
L1      2 (WEYFIAAEE|EYFIAAEEV)/SQSP AND 3-10/SQL
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9xx

=> d 1-2

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RN 499777-67-2 REGISTRY
ED Entered STN: 18 Mar 2003
CN L-Valine, L-tryptophyl-L- $\alpha$ -glutamyl-L-tyrosyl-L-phenylalanyl-L-
   isoleucyl-L-alanyl-L-alanyl-L- $\alpha$ -glutamyl-L- $\alpha$ -glutamyl- (9CI)
   (CA INDEX NAME)
OTHER NAMES:
CN 4: PN: US20030040600 SEQID: 6 claimed sequence
CN 6: PN: US20030040600 SEQID: 6 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C61 H81 N11 O18
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
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Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

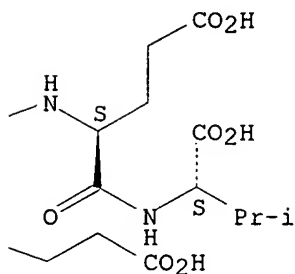
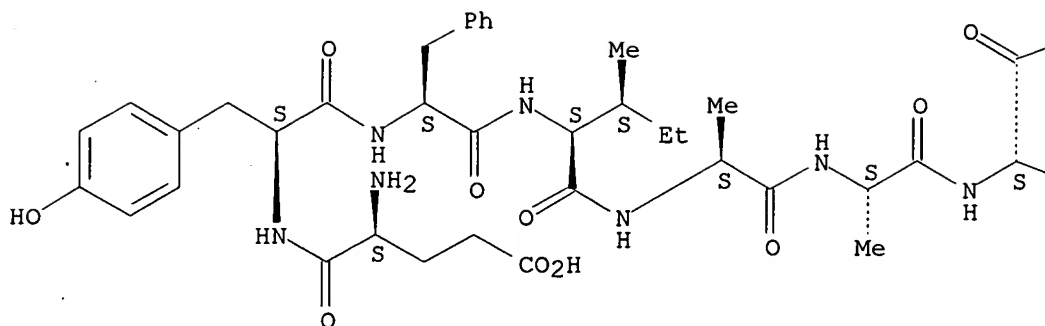
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 477192-10-2 REGISTRY
ED Entered STN: 19 Dec 2002
CN L-Valine, L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 22: PN: WO2005034844 SEQID: 24 unclaimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C50 H71 N9 O17
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
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FULL ESTIMATED COST

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FILE LAST UPDATED: 15 Sep 2005 (20050915/ED)

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=> s s1

L2 34303 S1

=> S L1

L3 3 L1

=> D BIB ABS 1-3

9xx

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:346796 CAPLUS

DN 142:406541

TI Hirudin-like peptides from C-terminus of human blood clotting factor Va heavy chain as prothrombinase inhibitors for use in treatment of blood clotting disorders

IN Kalafatis, Michael

Applicant

PA Cleveland State University, USA

SO PCT Int. Appl., 88 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005034844	A2	20050421	WO 2004-US21487	20040701
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	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI US 2003-502186P P 20030912

AB Disclosed are peptides from the carboxy terminus of the human blood clotting factor Va which significantly inhibit thrombin generation. Also disclosed are pharmaceutical compns. containing these peptides and related therapeutic methods for inhibiting thrombin generation and treating blood coagulation disorders. Thus, peptides DYDY and DYDQ, and sulfonated derivs. thereof, compete with prothrombinase for binding to prothrombin.

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

9xx

AN 2003:155110 CAPLUS

DN 138:198622

TI Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va as thrombin generation inhibitors

IN Kalafatis, Michael; Mann, Kenneth

Applicant

PA Cleveland State University, USA

SO U.S. Pat. Appl. Publ., 20 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003040600	A1	20030227	US 2001-911129	20010723

US 6703364 B2 20040309
US 2004186271 A1 20040923 US 2004-795795 20040308
PRAI US 2001-911129 A3 20010723

AB Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va are provided. Such peptides comprise: (i) a length of between 3 and 50 amino acids, (ii) a min. of 3 contiguous amino acids from the 307-356 heavy chain region of factor Va, excluding peptide segments comprising amino acids 311 to 325 and amino acids 321 to 335, (iii) optional addnl. amino acids at one or both ends of the contiguous amino acids such that the entire peptide is at least 60% identical to a sequence within 307 to 356 of factor Va, and (iv) have an IC50 of between 50 nM to 500 µM for inhibition of prothrombinase. The present invention also provides a pharmaceutical composition comprising one or more prothrombinase-inhibiting peptide segments. The present invention also provides administration of the pharmaceutical composition to human subjects for the purpose of preventing thrombotic disorders.

L3 ANSWER 3 OF 3, CAPLUS COPYRIGHT 2005 ACS on STN 9KX
AN 2002:732142 CAPLUS
DN 138:2631

TI Identification of a binding site for blood coagulation factor Xa on the heavy chain of factor Va. Amino acid residues 323-331 of factor V represent an interactive site for activated factor X

AU Kalafatis, Michael; Beck, Daniel O.

CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA

SO Biochemistry (2002), 41(42), 12715-12728 AFTER EFD
CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB The authors have recently shown that amino acid region 307-348 of factor Va heavy chain (42 amino acids, N42R) is critical for cofactor activity and may contain a binding site for factor Xa and/or prothrombin. To ascertain the importance of this region for factor Va cofactor activity, the authors have synthesized eight overlapping peptides (10 amino acid each) spanning amino acid region 307-351 of the heavy chain of factor Va and tested them for inhibition of prothrombinase activity. The peptides were also tested for the inhibition of the binding of factor Va to membrane-bound active site fluorescent labeled Glu-Gly-Arg human factor Xa ([OG488]-EGR-hXa). Factor Va binds specifically to membrane-bound [OG488]-EGR-hXa (10 nM) with half-maximum saturation reached at .apprx.6 nM. N42R was also found to interact with [OG488]-EGR-hXa with half-maximal saturation observed at .apprx.230

nM peptide. N42R was found to inhibit prothrombinase activity with an IC50 of .apprx.250 nM. A nonapeptide containing amino acid region 323-331 of factor Va (AP4') was found to be a potent inhibitor of prothrombinase. Kinetic analyses revealed that AP4' is a noncompetitive inhibitor of prothrombinase with respect to prothrombin, with a Ki of 5.7 µM. Thus, the peptide interferes with the factor Va-factor Xa interaction. Displacement expts. revealed that the nonapeptide inhibits the direct interaction of factor Va with [OG488]-EGR-hXa (IC50 .apprx.7.5 µM). The nonapeptide was also found to bind directly to [OG488]-EGR-hXa and to increase the catalytic efficiency of factor Xa toward prothrombin in the absence of factor Va. In contrast, a peptadecapeptide from N42R encompassing amino acid region 337-351 of factor Va (P15H) had no effect on either prothrombinase activity or the ability of the cofactor to interact with [OG488]-EGR-hXa. The authors' data demonstrate that amino acid sequence 323-331 of factor Va heavy chain contains a binding site for factor Xa.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
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822

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 * effective March 20, 2005. A new display format, IDERL, is now *
 * available and contains the CA role and document type information. *
 *

Structure search iteration limits have been increased. See HELP SLIMITS
 for details.

Experimental and calculated property data are now available. For more
 information enter HELP PROP at an arrow prompt in the file or refer
 to the file summary sheet on the web at:
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 583950 3-10/SQ L4
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=> D 1-2

L4 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 499777-67-2 REGISTRY
 ED Entered STN: 18 Mar 2003
 CN L-Valine, L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-
 isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI)
 (CA INDEX NAME)

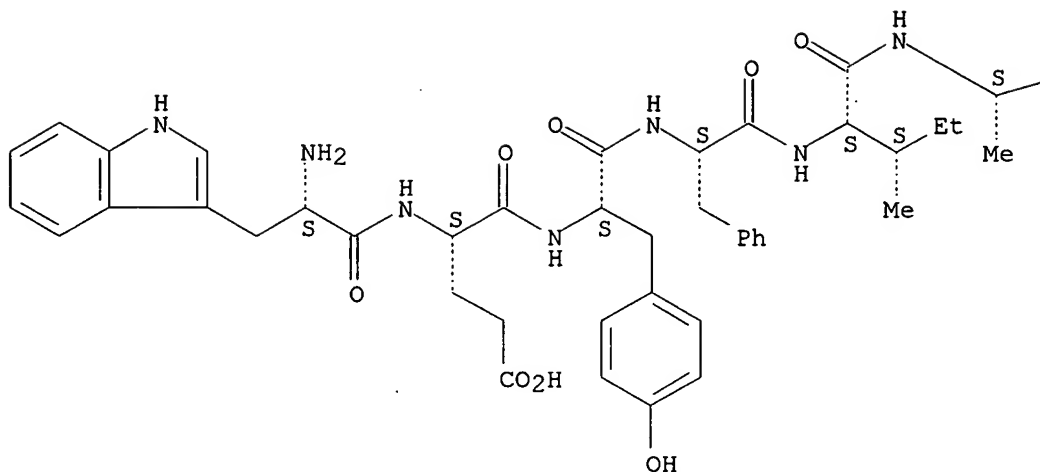
OTHER NAMES:

CN 4: PN: US20030040600 SEQID: 6 claimed sequence
 CN 6: PN: US20030040600 SEQID: 6 claimed protein
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C61 H81 N11 O18
 SR CA
 LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

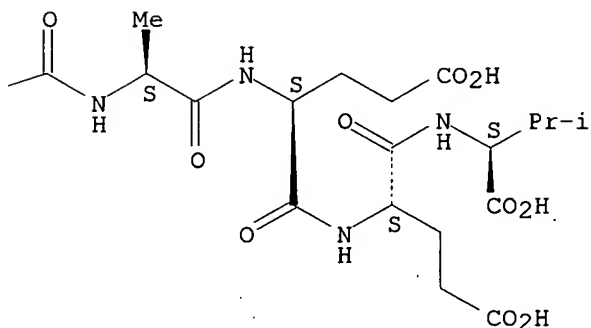
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Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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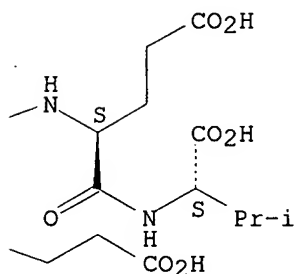
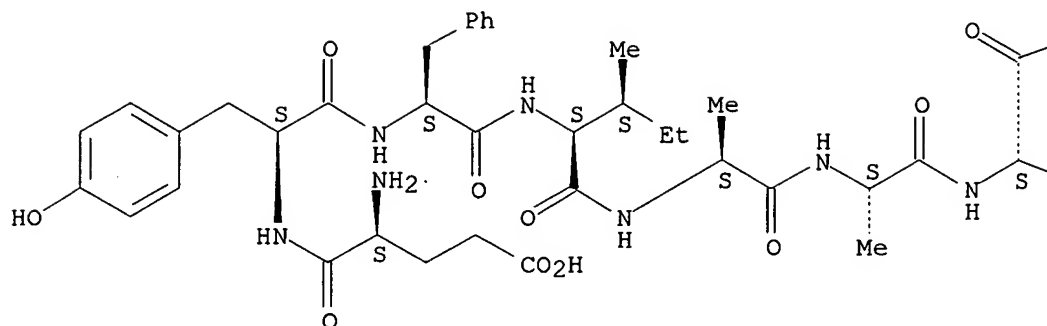
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 477192-10-2 REGISTRY
ED Entered STN: 19 Dec 2002
CN L-Valine, L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-
L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 22: PN: WO2005034844 SEQID: 24 unclaimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C50 H71 N9 O17
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



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2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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36.21	84.27

FULL ESTIMATED COST

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SINCE FILE ENTRY	TOTAL SESSION
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=> S L1

L5 3 L1

=> S L4

L6 3 L4

=> D BIB ABS 1-3

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN *Jua*
AN 2005:346796 CAPLUS
DN 142:406541
TI Hirudin-like peptides from C-terminus of human blood clotting factor Va
heavy chain as prothrombinase inhibitors for use in treatment of blood
clotting disorders
IN Kalafatis, Michael *Applicant*
PA Cleveland State University, USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005034844	A2	20050421	WO 2004-US21487	20040701
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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI US 2003-502186P P 20030912

AB Disclosed are peptides from the carboxy terminus of the human blood
clotting factor Va which significantly inhibit thrombin generation. Also
disclosed are pharmaceutical compns. containing these peptides and related
therapeutic methods for inhibiting thrombin generation and treating blood
coagulation disorders. Thus, peptides DYDY and DYDYQ, and sulfonated
derivs. thereof, compete with prothrombinase for binding to prothrombin.

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:155110 CAPLUS

DN 138:198622

TI Peptides derived from amino acids 307 to 356 of the human blood
coagulation factor Va as thrombin generation inhibitors

IN Kalafatis, Michael; Mann, Kenneth *Applicant*

PA Cleveland State University, USA

SO U.S. Pat. Appl. Publ., 20 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003040600	A1	20030227	US 2001-911129	20010723
	US 6703364	B2	20040309		
	US 2004186271	A1	20040923	US 2004-795795	20040308
PRAI	US 2001-911129	A3	20010723		
AB	<p>Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va are provided. Such peptides comprise: (i) a length of between 3 and 50 amino acids, (ii) a min. of 3 contiguous amino acids from the 307-356 heavy chain region of factor Va, excluding peptide segments comprising amino acids 311 to 325 and amino acids 321 to 335, (iii) optional addnl. amino acids at one or both ends of the contiguous amino acids such that the entire peptide is at least 60% identical to a sequence within 307 to 356 of factor Va, and (iv) have an IC50 of between 50 nM to 500 µM for inhibition of prothrombinase. The present invention also provides a pharmaceutical composition comprising one or more prothrombinase-inhibiting peptide segments. The present invention also provides administration of the pharmaceutical composition to human subjects for the purpose of preventing thrombotic disorders.</p>				

L6 ANSWER 3 OF 3, CAPLUS COPYRIGHT 2005 ACS on STN *VKX*
 AN 2002:732142 CAPLUS
 DN 138:2631

TI Identification of a binding site for blood coagulation factor Xa on the heavy chain of factor Va. Amino acid residues 323-331 of factor V represent an interactive site for activated factor X

AU Kalafatis, Michael; Beck, Daniel O.

CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA

SO Biochemistry (2002), 41(42), 12715-12728 *after EFD*
 CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB The authors have recently shown that amino acid region 307-348 of factor Va heavy chain (42 amino acids, N42R) is critical for cofactor activity and may contain a binding site for factor Xa and/or prothrombin. To ascertain the importance of this region for factor Va cofactor activity, the authors have synthesized eight overlapping peptides (10 amino acid each) spanning amino acid region 307-351 of the heavy chain of factor Va and tested them for inhibition of prothrombinase activity. The peptides were also tested for the inhibition of the binding of factor Va to membrane-bound active site fluorescent labeled Glu-Gly-Arg human factor Xa ([OG488]-EGR-hXa). Factor Va binds specifically to membrane-bound [OG488]-EGR-hXa (10 nM) with half-maximum saturation reached at .apprx.6 nM. N42R was also found to interact with [OG488]-EGR-hXa with half-maximal saturation observed at .apprx.230

nM peptide. N42R was found to inhibit prothrombinase activity with an IC50 of .apprx.250 nM. A nonapeptide containing amino acid region 323-331 of factor Va (AP4') was found to be a potent inhibitor of prothrombinase. Kinetic analyses revealed that AP4' is a noncompetitive inhibitor of prothrombinase with respect to prothrombin, with a Ki of 5.7 µM. Thus, the peptide interferes with the factor Va-factor Xa interaction. Displacement expts. revealed that the nonapeptide inhibits the direct interaction of factor Va with [OG488]-EGR-hXa (IC50 .apprx.7.5 µM). The nonapeptide was also found to bind directly to [OG488]-EGR-hXa and to increase the catalytic efficiency of factor Xa toward prothrombin in the absence of factor Va. In contrast, a peptadecapeptide from N42R encompassing amino acid region 337-351 of factor Va (P15H) had no effect on either prothrombinase activity or the ability of the cofactor to interact with [OG488]-EGR-hXa. The authors' data demonstrate that amino acid sequence 323-331 of factor Va heavy chain contains a binding site for factor Xa.

706

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=> file registry		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	8.40	92.67
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-2.19	-4.38

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STRUCTURE FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9
DICTIONARY FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

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conducting SmartSELECT searches.

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* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> S (WEYFIAA|EYFIAAE|YFIAAEE|FIAAEEV)/SQSP AND 3-10/SQ L7
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706

=> D 1-2

L7 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 499777-67-2 REGISTRY
ED Entered STN: 18 Mar 2003
CN L-Valine, L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-
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(CA INDEX NAME)

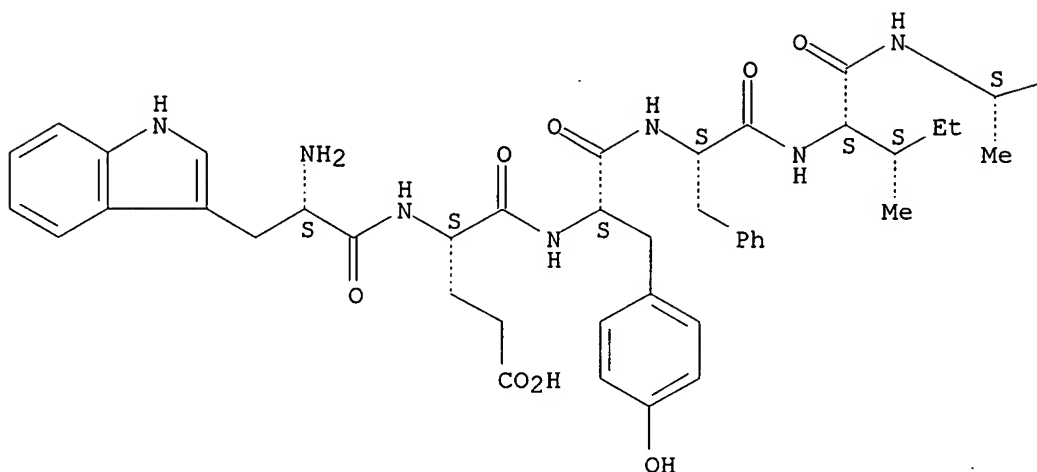
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CN 4: PN: US20030040600 SEQID: 6 claimed sequence
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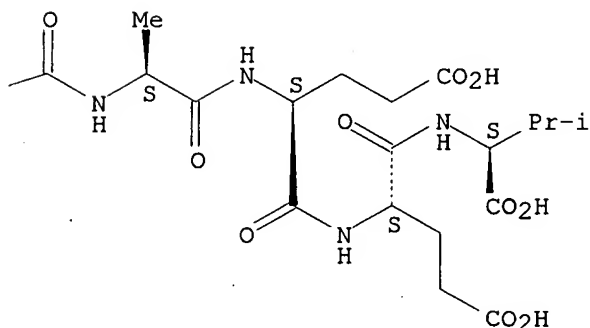
FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C61 H81 N11 O18
 SR CA
 LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

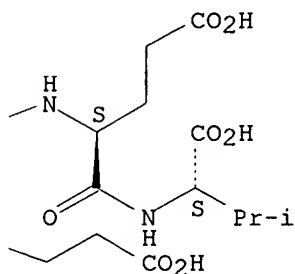
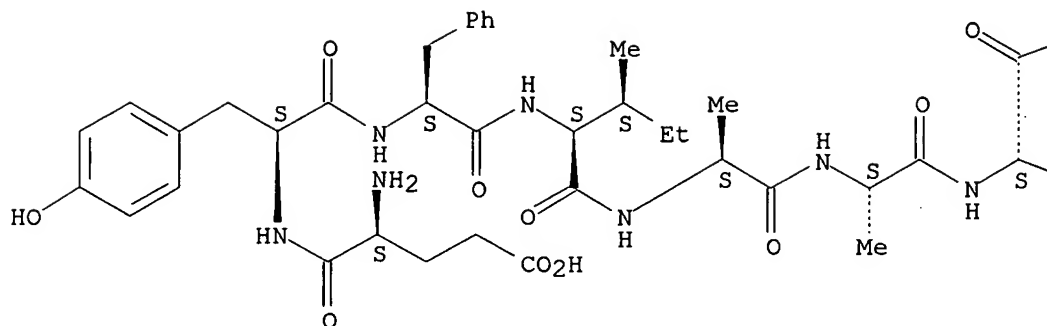
1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L7 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 477192-10-2 REGISTRY
 ED Entered STN: 19 Dec 2002
 CN L-Valine, L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 22: PN: WO2005034844 SEQID: 24 unclaimed sequence
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C50 H71 N9 O17
 SR CA
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file CAPLUS
COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
36.21	128.88

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
0.00	-4.38

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FILE COVERS 1907 - 16 Sep 2005 VOL 143 ISS 13
FILE LAST UPDATED: 15 Sep 2005 (20050915/ED)

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> S L7

L8 3 L7

=> D BIB ABS 1-3

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN 7XX
AN 2005:346796 CAPLUS
DN 142:406541
TI Hirudin-like peptides from C-terminus of human blood clotting factor Va
heavy chain as prothrombinase inhibitors for use in treatment of blood
clotting disorders
IN Kalafatis, Michael Applicant
PA Cleveland State University, USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005034844	A2	20050421	WO 2004-US21487	20040701
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	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI US 2003-502186P P 20030912

AB Disclosed are peptides from the carboxy terminus of the human blood clotting factor Va which significantly inhibit thrombin generation. Also disclosed are pharmaceutical compns. containing these peptides and related therapeutic methods for inhibiting thrombin generation and treating blood coagulation disorders. Thus, peptides DYDY and DYDYO, and sulfonated derivs. thereof, compete with prothrombinase for binding to prothrombin.

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN 7XX
AN 2003:155110 CAPLUS
DN 138:198622
TI Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va as thrombin generation inhibitors
IN Kalafatis, Michael; Mann, Kenneth Applicant
PA Cleveland State University, USA
SO U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 2003040600	A1	20030227	US 2001-911129	20010723
	US 6703364	B2	20040309		
	US 2004186271	A1	20040923	US 2004-795795	20040308
PRAI	US 2001-911129	A3	20010723		

AB Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va are provided. Such peptides comprise: (i) a length of between 3 and 50 amino acids, (ii) a min. of 3 contiguous amino acids from the 307-356 heavy chain region of factor Va, excluding peptide segments comprising amino acids 311 to 325 and amino acids 321 to 335, (iii) optional addnl. amino acids at one or both ends of the contiguous amino acids such that the entire peptide is at least 60% identical to a sequence within 307 to 356 of factor Va, and (iv) have an IC50 of between 50 nM to 500 μ M for inhibition of prothrombinase. The present invention also provides a pharmaceutical composition comprising one or more prothrombinase-inhibiting peptide segments. The present invention also provides administration of the pharmaceutical composition to human subjects for the purpose of preventing thrombotic disorders.

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN ~~700~~
 AN 2002:732142 CAPLUS

DN 138:2631

TI Identification of a binding site for blood coagulation factor Xa on the heavy chain of factor Va. Amino acid residues 323-331 of factor V represent an interactive site for activated factor X

AU Kalafatis, Michael; Beck, Daniel O.

CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA

SO Biochemistry (2002), 41(42), 12715-12728 ~~APPL EFD~~
 CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB The authors have recently shown that amino acid region 307-348 of factor Va heavy chain (42 amino acids, N42R) is critical for cofactor activity and may contain a binding site for factor Xa and/or prothrombin. To ascertain the importance of this region for factor Va cofactor activity, the authors have synthesized eight overlapping peptides (10 amino acid each) spanning amino acid region 307-351 of the heavy chain of factor Va and tested them for inhibition of prothrombinase activity. The peptides were also tested for the inhibition of the binding of factor Va to membrane-bound active site fluorescent labeled Glu-Gly-Arg human factor Xa ([OG488]-EGR-hXa). Factor Va binds specifically to membrane-bound [OG488]-EGR-hXa (10 nM) with half-maximum saturation reached at .apprx.6 nM. N42R was also found to interact with [OG488]-EGR-hXa with half-maximal saturation observed at .apprx.230

nM peptide. N42R was found to inhibit prothrombinase activity with an IC50 of .apprx.250 nM. A nonapeptide containing amino acid region 323-331 of factor Va (AP4') was found to be a potent inhibitor of prothrombinase. Kinetic analyses revealed that AP4' is a noncompetitive inhibitor of prothrombinase with respect to prothrombin, with a Ki of 5.7 μ M. Thus, the peptide interferes with the factor Va-factor Xa interaction. Displacement expts. revealed that the nonapeptide inhibits the direct interaction of factor Va with [OG488]-EGR-hXa (IC50 .apprx.7.5 μ M). The nonapeptide was also found to bind directly to [OG488]-EGR-hXa and to increase the catalytic efficiency of factor Xa toward prothrombin in the absence of factor Va. In contrast, a peptadecapeptide from N42R encompassing amino acid region 337-351 of factor Va (P15H) had no effect on either prothrombinase activity or the ability of the cofactor to interact with [OG488]-EGR-hXa. The authors' data demonstrate that amino acid sequence 323-331 of factor Va heavy chain contains a binding site for factor Xa.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

6028

=> file registry
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
8.40	137.28

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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STRUCTURE FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9
DICTIONARY FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> S (WEYFIA|EYFIAA|YFIAAE|FIAAEE|IAAEV)/SQSP AND 3-10/SQSP
2 WEYFIA|EYFIAA|YFIAAE|FIAAEE|IAAEV/SQSP
583950 3-10/SQSP
L9 2 (WEYFIA|EYFIAA|YFIAAE|FIAAEE|IAAEV)/SQSP AND 3-10/SQSP

=> D 1-2

L9 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 499777-67-2 REGISTRY
ED Entered STN: 18 Mar 2003
CN L-Valine, L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-
isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI)
(CA INDEX NAME)

OTHER NAMES:

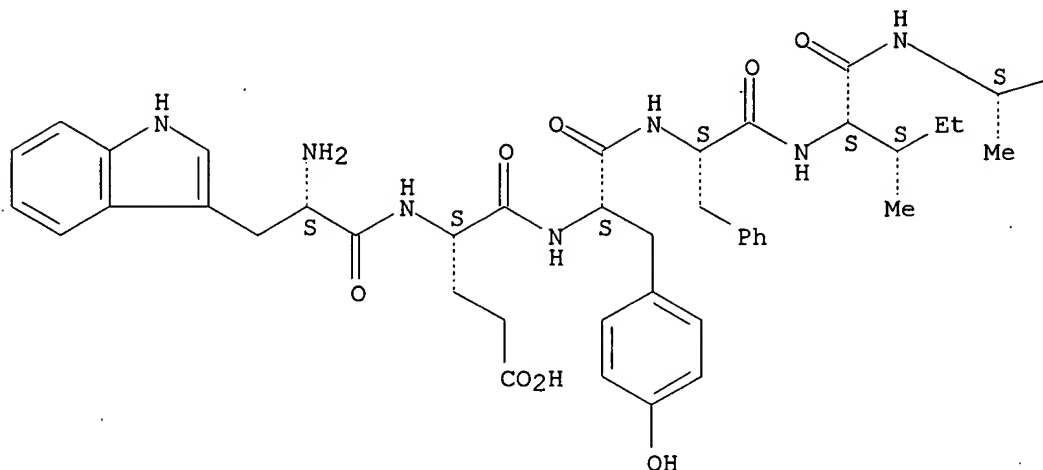
CN 4: PN: US20030040600 SEQID: 6 claimed sequence
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FS PROTEIN SEQUENCE; STEREOSEARCH
MF C61 H81 N11 O18
SR CA

6028

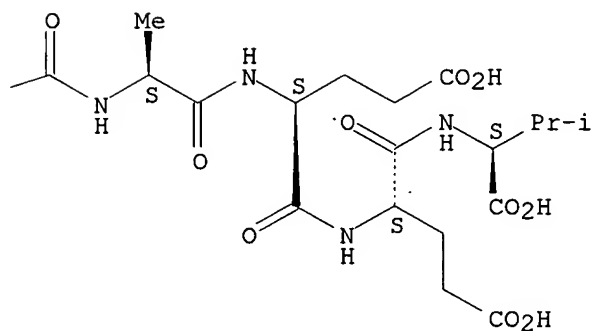
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

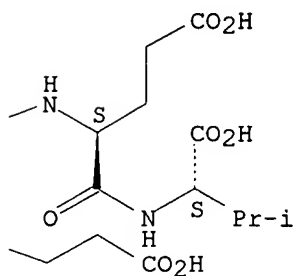
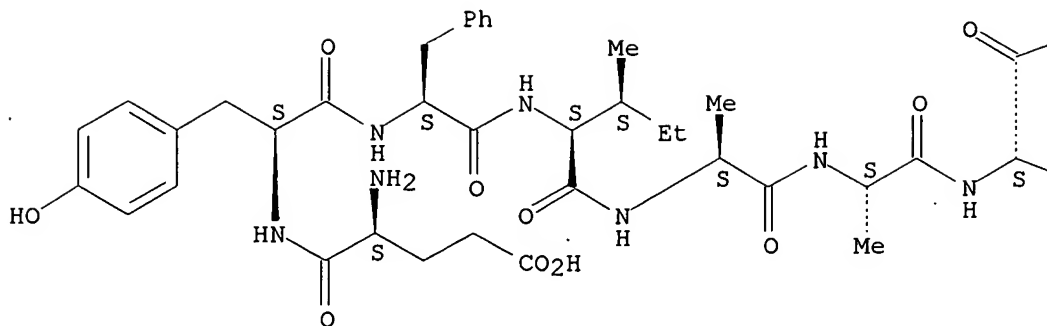


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 477192-10-2 REGISTRY
ED Entered STN: 19 Dec 2002
CN L-Valine, L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-
L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 22: PN: WO2005034844 SEQID: 24 unclaimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C50 H71 N9 O17
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
0.00	-6.57

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FILE COVERS 1907 - 16 Sep 2005 VOL 143 ISS 13
FILE LAST UPDATED: 15 Sep 2005 (20050915/ED)

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> S L9

L10 3 L9

=> D BIB ABS 1-3

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN *600*
AN 2005:346796 CAPLUS
DN 142:406541
TI Hirudin-like peptides from C-terminus of human blood clotting factor Va
heavy chain as prothrombinase inhibitors for use in treatment of blood
clotting disorders
IN Kalafatis, Michael *Applicant*
PA Cleveland State University, USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005034844	A2	20050421	WO 2004-US21487	20040701
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	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI US 2003-502186P P 20030912

AB Disclosed are peptides from the carboxy terminus of the human blood clotting factor Va which significantly inhibit thrombin generation. Also disclosed are pharmaceutical compns. containing these peptides and related therapeutic methods for inhibiting thrombin generation and treating blood coagulation disorders. Thus, peptides DYDY and DYDYQ, and sulfonated derivs. thereof, compete with prothrombinase for binding to prothrombin.

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN *600*
AN 2003:155110 CAPLUS
DN 138:198622
TI Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va as thrombin generation inhibitors
IN Kalafatis, Michael; Mann, Kenneth
PA Cleveland State University, USA *Applicant*
SO U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 2003040600	A1	20030227	US 2001-911129	20010723
	US 6703364	B2	20040309		
	US 2004186271	A1	20040923	US 2004-795795	20040308
PRAI	US 2001-911129	A3	20010723		

AB Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va are provided. Such peptides comprise: (i) a length of between 3 and 50 amino acids, (ii) a min. of 3 contiguous amino acids from the 307-356 heavy chain region of factor Va, excluding peptide segments comprising amino acids 311 to 325 and amino acids 321 to 335, (iii) optional addnl. amino acids at one or both ends of the contiguous amino acids such that the entire peptide is at least 60% identical to a sequence within 307 to 356 of factor Va, and (iv) have an IC50 of between 50 nM to 500 μ M for inhibition of prothrombinase. The present invention also provides a pharmaceutical composition comprising one or more prothrombinase-inhibiting peptide segments. The present invention also provides administration of the pharmaceutical composition to human subjects for the purpose of preventing thrombotic disorders.

L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN *6000*

AN 2002:732142 CAPLUS

DN 138:2631

TI Identification of a binding site for blood coagulation factor Xa on the heavy chain of factor Va. Amino acid residues 323-331 of factor V represent an interactive site for activated factor X

AU Kalafatis, Michael; Beck, Daniel O.

CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA

SO Biochemistry (2002), 41(42), 12715-12728 *After EFD*
CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB The authors have recently shown that amino acid region 307-348 of factor Va heavy chain (42 amino acids, N42R) is critical for cofactor activity and may contain a binding site for factor Xa and/or prothrombin. To ascertain the importance of this region for factor Va cofactor activity, the authors have synthesized eight overlapping peptides (10 amino acid each) spanning amino acid region 307-351 of the heavy chain of factor Va and tested them for inhibition of prothrombinase activity. The peptides were also tested for the inhibition of the binding of factor Va to membrane-bound active site fluorescent labeled Glu-Gly-Arg human factor Xa ([OG488]-EGR-hXa). Factor Va binds specifically to membrane-bound [OG488]-EGR-hXa (10 nM) with half-maximum saturation reached at .apprx.6 nM. N42R was also found to interact with [OG488]-EGR-hXa with half-maximal saturation observed at .apprx.230

nM peptide. N42R was found to inhibit prothrombinase activity with an IC50 of .apprx.250 nM. A nonapeptide containing amino acid region 323-331 of factor Va (AP4') was found to be a potent inhibitor of prothrombinase. Kinetic analyses revealed that AP4' is a noncompetitive inhibitor of prothrombinase with respect to prothrombin, with a Ki of 5.7 μ M. Thus, the peptide interferes with the factor Va-factor Xa interaction. Displacement expts. revealed that the nonapeptide inhibits the direct interaction of factor Va with [OG488]-EGR-hXa (IC50 .apprx.7.5 μ M). The nonapeptide was also found to bind directly to [OG488]-EGR-hXa and to increase the catalytic efficiency of factor Xa toward prothrombin in the absence of factor Va. In contrast, a peptadecapeptide from N42R encompassing amino acid region 337-351 of factor Va (P15H) had no effect on either prothrombinase activity or the ability of the cofactor to interact with [OG488]-EGR-hXa. The authors' data demonstrate that amino acid sequence 323-331 of factor Va heavy chain contains a binding site for factor Xa.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

500

=> file registry		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	8.40	181.89
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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CA SUBSCRIBER PRICE	-2.19	-8.76

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STRUCTURE FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9
 DICTIONARY FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when
 conducting SmartSELECT searches.

 *
 * The CA roles and document type information have been removed from *
 * the IDE default display format and the ED field has been added, *
 * effective March 20, 2005. A new display format, IDERL, is now *
 * available and contains the CA role and document type information. *
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Structure search iteration limits have been increased. See HELP SLIMITS
 for details.

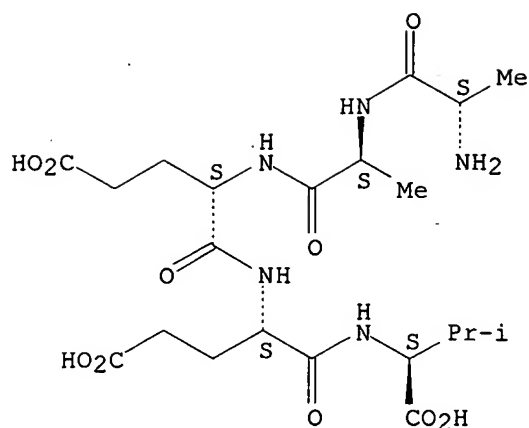
Experimental and calculated property data are now available. For more
 information enter HELP PROP at an arrow prompt in the file or refer
 to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> S (WEYFI|EYFIA|YFIAA|FIAAE|IAAEE|AAEEV|LDNFS)/SQSP AND 3-10/SQL
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 583950 3-10/SQL
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L11 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 603110-44-7 REGISTRY
 ED Entered STN: 13 Oct 2003
 CN L-Valine, L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI)
 (CA INDEX NAME)
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 SR CA
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.



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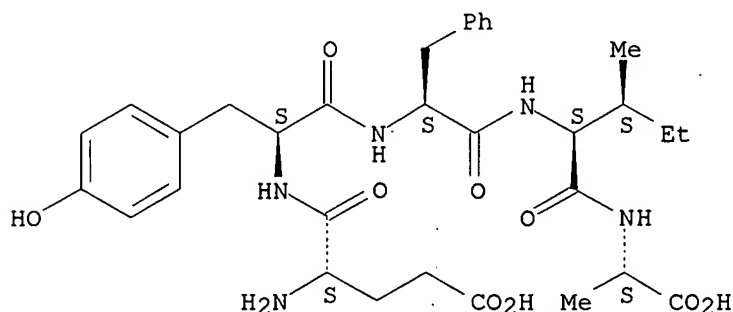
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
RN 603110-42-5 REGISTRY
ED Entered STN: 13 Oct 2003
CN L-Alanine, L-α-glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl- (9CI)
(CA INDEX NAME)

OTHER NAMES:

CN 23: PN: WO2005034844 SEQID: 25 unclaimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H43 N5 O9
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



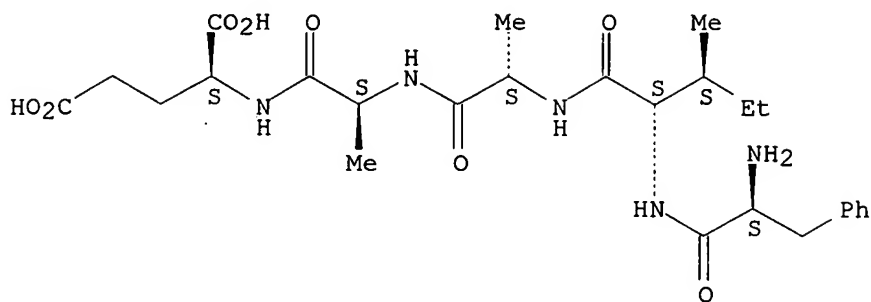
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
RN 603110-41-4 REGISTRY
ED Entered STN: 13 Oct 2003
CN L-Glutamic acid, L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl- (9CI) (CA
INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C26 H39 N5 O8
SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN

RN 503587-58-4 REGISTRY

ED Entered STN: 22 Apr 2003

CN L-Arginine, L-tyrosyl-L-leucyl-L- α -aspartyl-L-asparaginyl-L-phenylalanyl-L-seryl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 93: PN: WO03025005 FIGURE: 43 unclaimed sequence

FS PROTEIN SEQUENCE; STEREOSEARCH

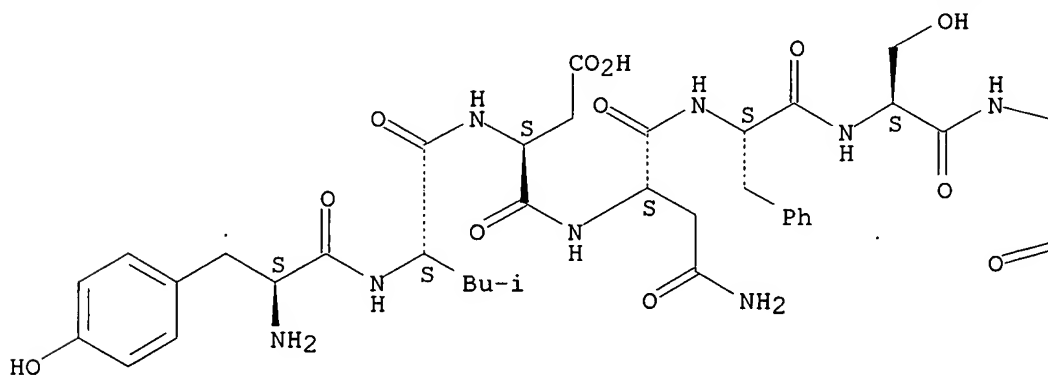
MF C51 H73 N13 O19

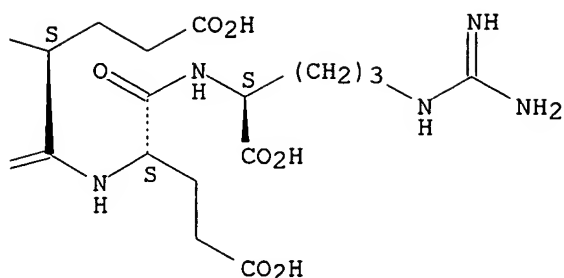
SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

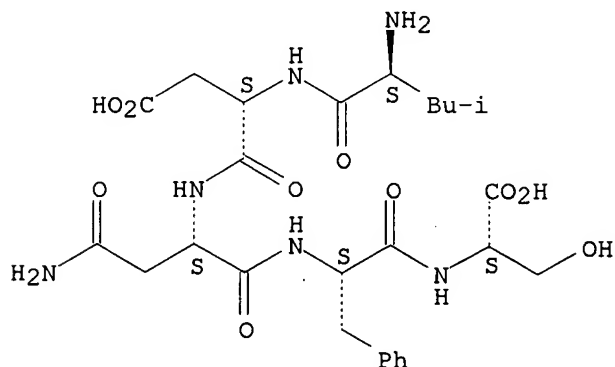
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
RN 499777-73-0 REGISTRY
ED Entered STN: 18 Mar 2003
CN L-Serine, L-leucyl-L-α-aspartyl-L-asparaginyl-L-phenylalanyl- (9CI)
(CA INDEX NAME)

OTHER NAMES:

CN 10: PN: US20030040600 SEQID: 12 claimed sequence
CN 12: PN: US20030040600 SEQID: 12 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C26 H38 N6 O10
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

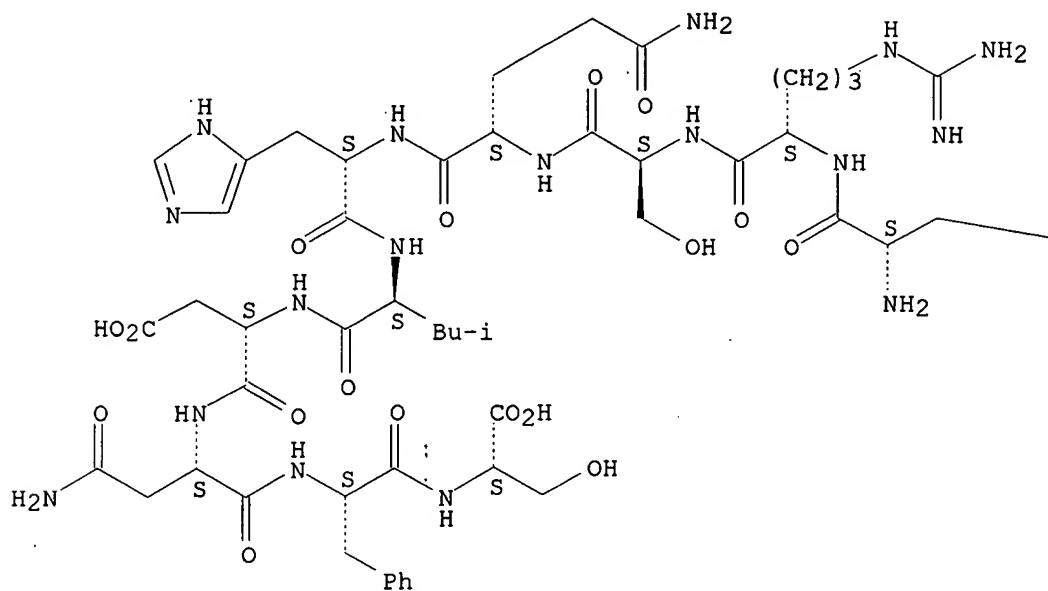
L11 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
RN 499777-72-9 REGISTRY
ED Entered STN: 18 Mar 2003
CN L-Serine, L-tyrosyl-L-arginyl-L-seryl-L-glutaminyl-L-histidyl-L-leucyl-L-α-aspartyl-L-asparaginyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

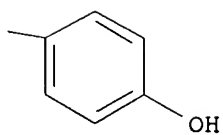
CN 11: PN: US20030040600 SEQID: 11 claimed protein
 CN 9: PN: US20030040600 SEQID: 11 claimed sequence
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C55 H79 N17 O18
 SR CA
 LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
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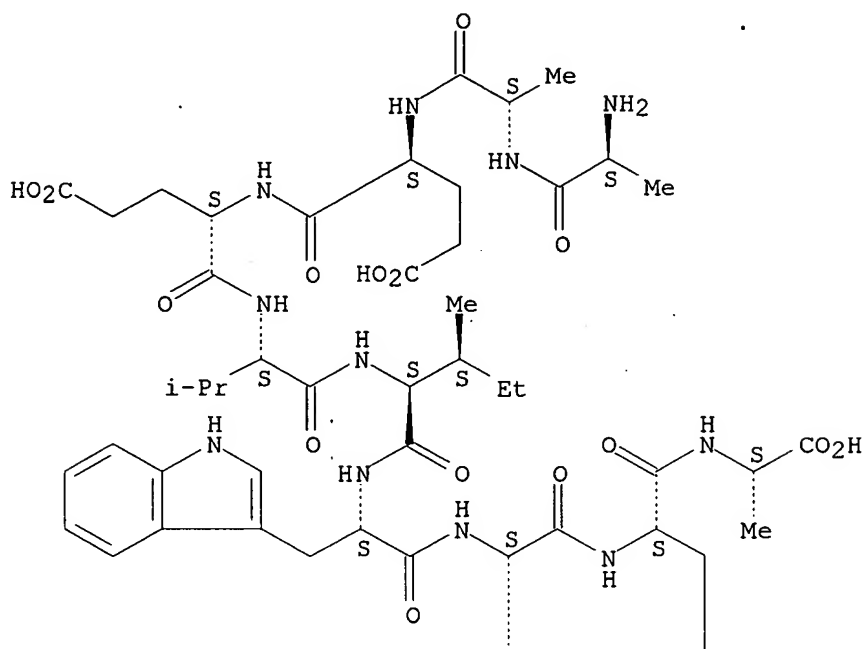
L11 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 499777-68-3 REGISTRY
 ED Entered STN: 18 Mar 2003
 CN L-Alanine, L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl-L-valyl-
 L-isoleucyl-L-tryptophyl-L- α -aspartyl-L-tyrosyl- (9CI) (CA INDEX
 NAME)

OTHER NAMES:

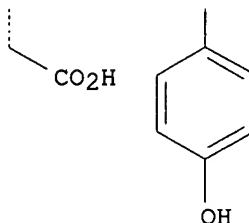
CN 5: PN: US20030040600 SEQID: 7 claimed sequence
 CN 7: PN: US20030040600 SEQID: 7 claimed protein
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C54 H75 N11 O18
 SR CA
 LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 499777-67-2 REGISTRY
 ED Entered STN: 18 Mar 2003
 CN L-Valine, L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI)
 (CA INDEX NAME)

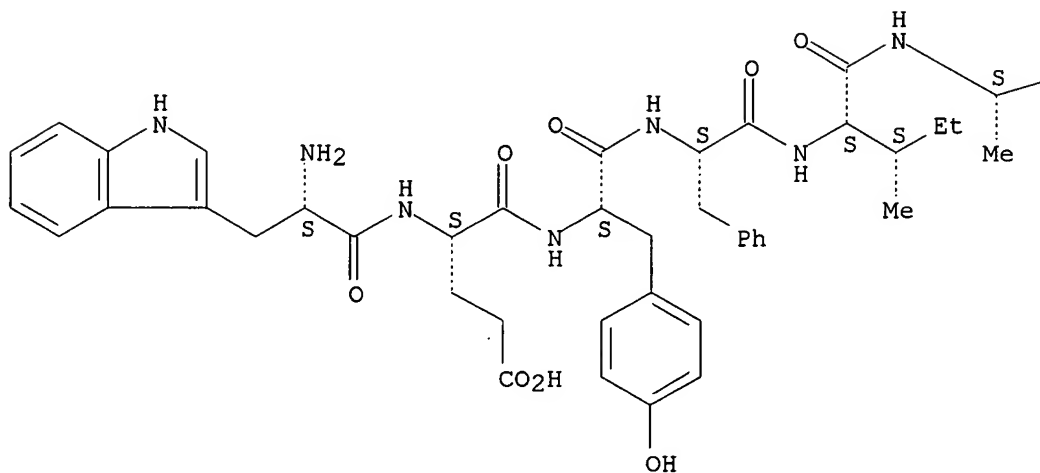
OTHER NAMES:

CN 4: PN: US20030040600 SEQID: 6 claimed sequence

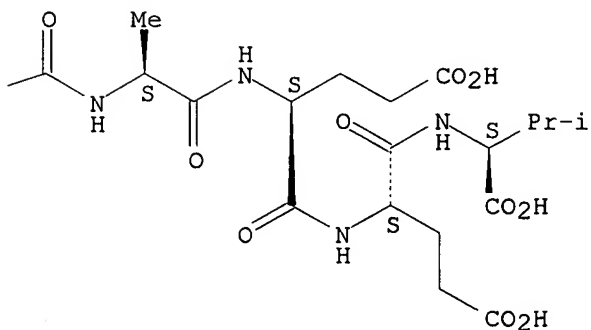
CN 6: PN: US20030040600 SEQID: 6 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C61 H81 N11 O18
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN

RN 499777-66-1 REGISTRY

ED Entered STN: 18 Mar 2003

CN L-Isoleucine, L-arginyl-L-histidyl-L-methionyl-L-lysyl-L-arginyl-L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 3: PN: US20030040600 SEQID: 5 claimed sequence

CN 5: PN: US20030040600 SEQID: 5 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C69 H100 N20 O14 S

SR CA

Absolute stereochemistry.

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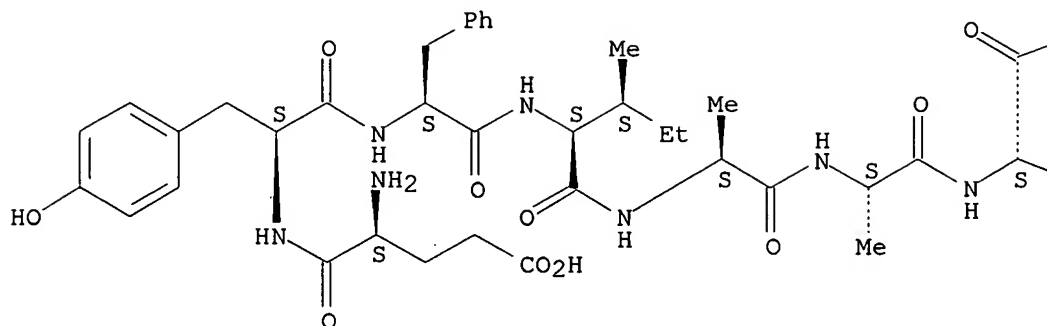
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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RN   477192-10-2  REGISTRY
ED   Entered STN:   19 Dec 2002
CN   L-Valine, L- $\alpha$ -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-
      L-alanyl-L- $\alpha$ -glutamyl-L- $\alpha$ -glutamyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   22: PN: WO2005034844 SEQID: 24 unclaimed sequence
FS   PROTEIN SEQUENCE; STEREOSEARCH
MF   C50 H71 N9 O17
SR   CA
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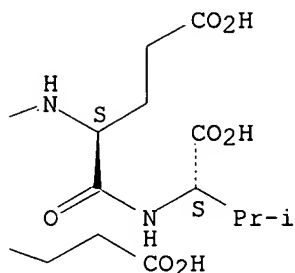
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
RN 321875-41-6 REGISTRY
ED Entered STN: 15 Feb 2001
CN L-Tryptophan, L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl-L-asparaginyl- (9CI) (CA INDEX NAME)

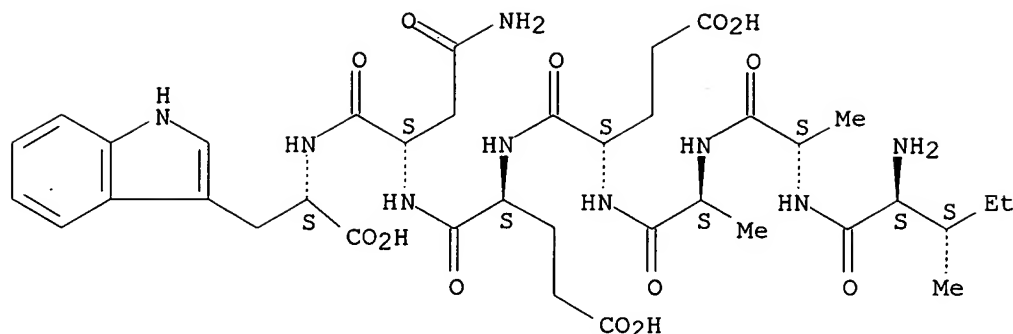
OTHER NAMES:

CN 1126: PN: WO0104316 PAGE: 63 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C37 H53 N9 O13
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

WIA AEE N
= 326-330
of Factor Va

ORF 41a?



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file CAPLUS
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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FILE LAST UPDATED: 15 Sep 2005 (20050915/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L11
L12 6 L11

=> D BIB ABS 1-6

5xx

L12 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:346796 CAPLUS
DN 142:406541
TI Hirudin-like peptides from C-terminus of human blood clotting factor Va heavy chain as prothrombinase inhibitors for use in treatment of blood clotting disorders
IN Kalafatis, Michael

Applicant

PA Cleveland State University, USA
 SO PCT Int. Appl., 88 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005034844	A2	20050421	WO 2004-US21487	20040701
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI US 2003-502186P P 20030912

AB Disclosed are peptides from the carboxy terminus of the human blood clotting factor Va which significantly inhibit thrombin generation. Also disclosed are pharmaceutical compns. containing these peptides and related therapeutic methods for inhibiting thrombin generation and treating blood coagulation disorders. Thus, peptides DYDY and DYDQ, and sulfonated derivs. thereof, compete with prothrombinase for binding to prothrombin.

L12 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN 500

AN 2003:556837 CAPLUS

DN 139:257136

TI Amino Acids Glu323, Tyr324, Glu330, and Val331 of Factor Va Heavy Chain Are Essential for Expression of Cofactor Activity

AU Singh, Lisam S.; Bukys, Michael A.; Beck, Daniel O.; Kalafatis, Michael

CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA

SO Journal of Biological Chemistry (2003), 278(30), 28335-28345 AFTER EFD
 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB We have recently demonstrated that amino acid region 323-331 of factor Va heavy chain (9 amino acids, AP4') contains a binding site for factor Xa (Kalafatis, M., and Beck, D. O. (2002) Biochem. 41, 12715-12728). To ascertain which amino acids within this region are important for the effector and receptor properties of the cofactor with respect to factor Xa, we have synthesized three overlapping peptides (5 amino acids each) spanning the amino acid region 323-331 and tested them for their effect on prothrombinase complex assembly and function. Peptide containing amino acids 323EYFIA327 alone was found to increase the catalytic efficiency of factor Xa but had no effect on the fluorescent anisotropy of active site-labeled factor Xa (human factor Xa labeled in the active site with Oregon Green 488; [OG488]-EGR-hXa). In contrast, peptide containing the sequence 327AAEEV331 was found to interact with [OG488]-EGR-hXa with half-maximal saturation reached at .apprx.150 μ M, but it was unable to produce a cofactor effect on factor Xa. Peptide 325FIAAE329 inhibited prothrombinase activity and was able to partially decrease the fluorescent anisotropy of [OG488]-EGR-hXa but could not increase the catalytic efficiency of factor Xa with respect to prothrombin. A control peptide with the sequence FFFIA did not increase the catalytic efficiency of factor Xa, whereas a peptide with the sequence Emi was impaired in its capability to interact with [OG488]-EGR-hXa. Two mutant recombinant factor Va mols. (Glu323 Phe/Tyr324 Phe, factor VaFF; Glu330 Met/Val331 Ile, factor VaMI) showed impaired cofactor activity when used at limiting cofactor concentration, whereas

the quadruple mutant (Glu323 Phe/Tyr324 Phe and Glu330 Met/Val331Ile, factor VaFF/MI) had no cofactor activity under similar exptl. conditions. Our data demonstrate that amino acid residues Glu323, Tyr324, Glu330, and Val331 of factor Va heavy chain are critical for expression of factor Va cofactor activity.

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN Sdx

AN 2003:242369 CAPLUS

DN 138:283309

TI Cloning, purification and characterization of enzymes from pathogenic bacteria involved in protein processing and drug screening and drug design applications

IN Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Alam, Muhammad Zahoor; Awrey, Donald; Beattie, Bryan; Canadien, Veronica; Domagala, Megan; Kanagarajah, Dhushy; Li, Qin; Mansoury, Kamran; Necakov, Sasha; Nethery, Kathleen; Ng, Ivy; Pinder, Benjamin; Sheldrick, Bay; Vallee, Francois; Viola, Cristina; Wrezel, Olga; et al.

PA Affinium Pharmaceuticals, Inc., Can.

SO PCT Int. Appl., 273 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003025005	A2	20030327	WO 2002-CA1426	20020920
	WO 2003025005	A3	20040311		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRAI	US 2001-324135P	P	20010921		
	US 2001-324139P	P	20010921		
	US 2001-325333P	P	20010927		
	US 2001-325836P	P	20010928		
	US 2001-338235P	P	20011025		
	US 2001-343758P	P	20011025		
	US 2001-340531P	P	20011026		
	US 2001-340945P	P	20011030		
	US 2001-333281P	P	20011106		
	US 2002-399926P	P	20020731		

After EFD

AB The present invention relates to polypeptide targets for pathogenic bacteria. A number of antimicrobial target enzymes have been identified, expressed, and purified from Staphylococcus aureus, Helicobacter pylori, Streptococcus pneumoniae, and Escherichia coli. Cloning, the nucleotide sequences and the encoded amino acid sequences of genes clpL, cysM, pepP, kdsA, secA, trmD, ilvE, aroB, and glyA from S. aureus, H. pylori, S. pneumoniae, and E. coli are disclosed. The invention also provides biochem. and biophys. characteristics of those polypeptides. The polypeptides are characterized by using mass spectrometry, NMR, x-ray crystallog., and bioinformatics anal. The polypeptides of the invention can be used for drug screening, drug design, in diagnostic assays and in pharmacol. applications.

L12 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:155110 CAPLUS

DN 138:198622
TI Peptides derived from amino acids 307 to 356 of the human blood *Sxx*
coagulation factor Va as thrombin generation inhibitors
IN Kalafatis, Michael; Mann, Kenneth
PA Cleveland State University, USA *Applicant*
SO U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO

DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003040600	A1	20030227	US 2001-911129	20010723
	US 6703364	B2	20040309		
	US 2004186271	A1	20040923	US 2004-795795	20040308
PRAI	US 2001-911129	A3	20010723		

AB Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va are provided. Such peptides comprise: (i) a length of between 3 and 50 amino acids, (ii) a min. of 3 contiguous amino acids from the 307-356 heavy chain region of factor Va, excluding peptide segments comprising amino acids 311 to 325 and amino acids 321 to 335, (iii) optional addnl. amino acids at one or both ends of the contiguous amino acids such that the entire peptide is at least 60% identical to a sequence within 307 to 356 of factor Va, and (iv) have an IC50 of between 50 nM to 500 μ M for inhibition of prothrombinase. The present invention also provides a pharmaceutical composition comprising one or more prothrombinase-inhibiting peptide segments. The present invention also provides administration of the pharmaceutical composition to human subjects for the purpose of preventing thrombotic disorders.

L12 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN *Sxx*
AN 2002:732142 CAPLUS

DN 138:2631

TI Identification of a binding site for blood coagulation factor Xa on the heavy chain of factor Va. Amino acid residues 323-331 of factor V represent an interactive site for activated factor X

AU Kalafatis, Michael; Beck, Daniel O.

CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA

SO Biochemistry (2002), 41(42), 12715-12728 *After EFD*
CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB The authors have recently shown that amino acid region 307-348 of factor Va heavy chain (42 amino acids, N42R) is critical for cofactor activity and may contain a binding site for factor Xa and/or prothrombin. To ascertain the importance of this region for factor Va cofactor activity, the authors have synthesized eight overlapping peptides (10 amino acid each) spanning amino acid region 307-351 of the heavy chain of factor Va and tested them for inhibition of prothrombinase activity. The peptides were also tested for the inhibition of the binding of factor Va to membrane-bound active site fluorescent labeled Glu-Gly-Arg human factor Xa ([OG488]-EGR-hXa). Factor Va binds specifically to membrane-bound [OG488]-EGR-hXa (10 nM) with half-maximum saturation reached at .apprx.6 nM. N42R was also found to interact with [OG488]-EGR-hXa with half-maximal saturation observed at .apprx.230

nM peptide. N42R was found to inhibit prothrombinase activity with an IC50 of .apprx.250 nM. A nonapeptide containing amino acid region 323-331 of factor Va (AP4') was found to be a potent inhibitor of prothrombinase. Kinetic analyses revealed that AP4' is a noncompetitive inhibitor of prothrombinase with respect to prothrombin, with a Ki of 5.7 μ M. Thus, the peptide interferes with the factor Va-factor Xa interaction. Displacement expts. revealed that the nonapeptide inhibits the direct

interaction of factor Va with [OG488]-EGR-hXa (IC50 .apprx.7.5 µM). The nonapeptide was also found to bind directly to [OG488]-EGR-hXa and to increase the catalytic efficiency of factor Xa toward prothrombin in the absence of factor Va. In contrast, a peptadecapeptide from N42R encompassing amino acid region 337-351 of factor Va (P15H) had no effect on either prothrombinase activity or the ability of the cofactor to interact with [OG488]-EGR-hXa. The authors' data demonstrate that amino acid sequence 323-331 of factor Va heavy chain contains a binding site for factor Xa.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN 500

AN 2001:50820 CAPLUS

DN 134:126821

TI Antigenic determinants of antigenic proteins of Neisseria meningitidis and their diagnostic, prophylactic and therapeutic use

IN Masignani, Vega; Scarlato, Vincenzo; Scarselli, Maria; Galeotti, Cesira; Mora, Mariarosa

PA Chiron S.p.A., Italy

SO PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	WO 2001004316	A3	20010809.		
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	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	CA 2378547	AA	20010118	CA 2000-2378547	20000713
	EP 1196587	A2	20020417	EP 2000-944161	20000713
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO		
	BR 2000012424	A	20020702	BR 2000-12424	20000713
	JP 2003504062	T2	20030204	JP 2001-509520	20000713
	RU 2253678	C2	20050610	RU 2002-103604	20000713
X PRAI	GB 1999-16529	A	19990714		
	WO 2000-IB1026	W	20000713	GB 9916529.2 102B *	

AB Antigenic determinants of known antigenic proteins of Neisseria meningitidis are characterized. The peptides can be used as diagnostic reagents or as antigens for vaccines and they may be manufactured by expression of a natural or synthetic gene encoding the protein. Homologous sequences and proteins comprising these fragments are also disclosed.

=> file registry

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

16.35

251.01

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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DICTIONARY FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9

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* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> S (WEYF|EYFI|YFIA|FIAA|IAAE|AAEE|AEEV|LDNF|DNFS)/SQSP AND 3-10/SQSP
170 WEYF|EYFI|YFIA|FIAA|IAAE|AAEE|AEEV|LDNF|DNFS/SQSP
583950 3-10/SQSP
L13 170 (WEYF|EYFI|YFIA|FIAA|IAAE|AAEE|AEEV|LDNF|DNFS)/SQSP AND 3-10/SQSP

400

=> file CAPLUS

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	32.53	283.54
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-13.14

FILE 'CAPLUS' ENTERED AT 13:51:45 ON 16 SEP 2005
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302

FILE COVERS 1907 - 16 Sep 2005 VOL 143 ISS 13
FILE LAST UPDATED: 15 Sep 2005 (20050915/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L13

L14 121 L13

4XX

=> file registry

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.45

283.99

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-13.14

FILE 'REGISTRY' ENTERED AT 13:52:03 ON 16 SEP 2005

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9

DICTIONARY FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> S (WEY|EYF|YFI|FIA|IAA|AAE|AEE|EEV|LDN|DNF|NFS)/SQSP AND 3-10/SQ

4544 WEY|EYF|YFI|FIA|IAA|AAE|AEE|EEV|LDN|DNF|NFS/SQSP

583950 3-10/SQ

L15 4544 (WEY|EYF|YFI|FIA|IAA|AAE|AEE|EEV|LDN|DNF|NFS)/SQSP AND 3-10/SQ

=> file CAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

32.53

316.52

302

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-13.14

FILE 'CAPLUS' ENTERED AT 13:52:40 ON 16 SEP 2005
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FILE COVERS 1907 - 16 Sep 2005 VOL 143 ISS 13
 FILE LAST UPDATED: 15 Sep 2005 (20050915/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L15

L16 1915 L15 3αα

=> dis his

(FILE 'HOME' ENTERED AT 13:43:24 ON 16 SEP 2005)

L1 FILE 'REGISTRY' ENTERED AT 13:43:38 ON 16 SEP 2005
 2 S (WEYFIAAEE|EYFIAAEEV)/SQSP AND 3-10/SQL

L2 FILE 'CAPLUS' ENTERED AT 13:44:13 ON 16 SEP 2005
 34303 S S1
 L3 3 S L1

L4 FILE 'REGISTRY' ENTERED AT 13:46:19 ON 16 SEP 2005
 2 S (WEYEIAAE|EYFIAAEE|YFIAAEEV)/SQSP AND 3-10/SQL

L5 FILE 'CAPLUS' ENTERED AT 13:47:02 ON 16 SEP 2005
 3 S L1
 L6 3 S L4

L7 FILE 'REGISTRY' ENTERED AT 13:47:52 ON 16 SEP 2005
 2 S (WEYFIAA|EYFIAAEE|YFIAAEE|FIAAEEV)/SQSP AND 3-10/SQL

L8 FILE 'CAPLUS' ENTERED AT 13:48:34 ON 16 SEP 2005
 3 S L7

L9 FILE 'REGISTRY' ENTERED AT 13:48:53 ON 16 SEP 2005
 2 S (WEYFIA|EYFIAA|YFIAAEE|FIAAEE|IAAEEV)/SQSP AND 3-10/SQL

L10 FILE 'CAPLUS' ENTERED AT 13:49:41 ON 16 SEP 2005
 3 S L9

L11 FILE 'REGISTRY' ENTERED AT 13:50:08 ON 16 SEP 2005
 11 S (WEYFI|EYFIA|YFIAA|FIAAEE|IAAEEV|LDNFS)/SQSP AND 3-10/SQL

L12 FILE 'CAPLUS' ENTERED AT 13:50:44 ON 16 SEP 2005
6 S L11

L13 FILE 'REGISTRY' ENTERED AT 13:51:08 ON 16 SEP 2005
170 S (WEYF|EYFI|YFIA|FIAA|IAAE|AAEE|AEEV|LDNF|DNFS)/SQSP AND 3-10/

L14 FILE 'CAPLUS' ENTERED AT 13:51:45 ON 16 SEP 2005
121 S L13

L15 FILE 'REGISTRY' ENTERED AT 13:52:03 ON 16 SEP 2005
4544 S (WEY|EYF|YFI|FIA|IAA|AAE|AEE|EEV|LDN|DNF|NFS)/SQSP AND 3-10/S

L16 FILE 'CAPLUS' ENTERED AT 13:52:40 ON 16 SEP 2005
1915 S L15

=> logoff

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD: y

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.45	316.97

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
0.00	-13.14

CA SUBSCRIBER PRICE

STN INTERNATIONAL LOGOFF AT 13:53:28 ON 16 SEP 2005

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:sssptal652mxm

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

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NEWS 8 SEP 09 ACD predicted properties enhanced in REGISTRY/ZREGISTRY

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MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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FILE 'HOME' ENTERED AT 07:04:49 ON 16 SEP 2005

=> s deltrophin##

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Some commands only work in certain files. For example, the EXPAND
command can only be used to look at the index in a file which has an
index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 07:05:33 ON 16 SEP 2005

FILE 'EMBASE' ENTERED AT 07:05:33 ON 16 SEP 2005
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W 795775

5

352-LDNFS-356

1 2 3 4 5 6 7 8 9 10

322-WEYFIAAEEV-331

WEYFIAAEE
EYFIAAEEV = 9

WEYEIAAE
EYFIAAEE = 8
YFIAAEEV

WEYFIAA
EYFIAAE
YFIAAEE = 7
FIAAEEV

WEYFIA
EYFIAA
YFIAAE
FIAAEE = 6
IAAEEV

S → done by Jon

WEYF LDNF
EYFI DNFS
YFIA = 4
FIAA
IAAE
AAEE
AEEV

WEY LDN
EYF DNFS = 3
YFI
FIA
IAA
AAE
AEE
EEV